D' Cont.

74. Tablet according to claim 63, wherein the sweetener is selected from the group consisting of aspartame, potassium acesulfame, sodium saccharinate, neohesperidin dihydrochalcone and mixtures thereof.

REMARKS

New claims 48 and 61, which correspond respectively to former claims 21 and 34, have been amended to specify that:

The mixture of excipients is free of effervescent agents,

The active ingredient is no intimately dispersed or dissolved in a pharmaceutically acceptable lipid.

Former claims 22 to 33 have been renumbered 49 to 60, and their dependencies have been amended consequently.

Former claims 35 to 48 have been renumbered 62 to 74, and their dependencies have been amended consequently.

The Examiner maintains his objections under 35 USC 103(a) as being unpatentable over Ghanta et al. (US 5814332) in view of Gegerly et al. (US 5064656).

Applicants respectfully traverse this ground of objection.

The Examiner indicates that Ghanta et al. describes a tablet which presents the same components than the tablet according to the invention.

In fact, tablets according to Ghanta are intended to mask the bitter taste of some active substances, for example ibuprofen.

In order to obtain the desired taste masking, the tablet according to Ghanta can present the same components as those used in the tablet according to the invention. However, the proportions of the different components are not the same. And in particular, the amount of disintegrating agent in Ghanta is very low.

The Examiner further indicates that Gegerly *"is used to show that proportions can be manipulated to yield the desired dissolution time."*

However, the man skilled in the art would never combine Ghanta with Gergely to obtain tablet which disintegrate in the mouth in less than 40 s, and in which the particles of active principle are coated.

Firstly, Gergely concerns effervescent tablets while tablets according to the invention are free of effervescent agents.

Secondly, the Applicants respectfully disagree with the Examiner when he indicates that *"Gergely teaches two reactants can be coated with disintegrating agents on column 13, line 49"*.

In fact, in Gergely, the term "reactants" refer to the effervescent agents, as it is expressly mentioned at column 2 lines 49-50) and not to the pharmaceutically active substance.

Thus, Gergely does not describe nor suggest coated particles of active principle.

Thirdly, the dissolution time which is measured in this document is a dissolution time in water as it results from the whole description and more specifically from example 40, while in the invention the dissolution time is the dissolution in the saliva in the mouth.

Thus, Gegerly teaches away from the invention.

Nothing incites the person skilled in the art to combine Ghanta et al. with Gegerly et al.

Even if these documents were combined they would not suggest the tablet according to the invention. In particular, the required proportion of disintegrating agent could in no way be deduced from Gergely.

The only proportions which are indicated to be manipulated in Gergely are the proportions of effervescent reactants relative to disintegrating agents, as it comes from column 8 lines 28-35 and examples 10-14.

Further, at column 6 line 45, Gegerly indicates that if the amount of disintegrant is increased, the tablet does not disintegrate faster, but significantly slower.

This assertion is confirmed at column 15 line 15, where it is indicated in the case of Ibuprofen that *"the weight ratio of disintegrant to reactant can be reduced mainly (....) in the case of ibuprofen."*

In view of these assertions, the man skilled in the art would tend to decrease and not to increase the amount of disintegrating agent present in Ghanta tablets.

Claims 48 and 61 are thus inventive over Ghanta et al. in view of Gergely et al.

Since claims 49 to 60 depend on claim 48 and since claims 62 to 74 depend on claim 61, they are also inventive.

The Examiner maintains his objections under 35 USC 103(a) as being unpatentable over Geyer et al. (US 5320848) in view of Meyers et al. (US 5567439).

Applicants respectfully traverse this ground of objection.

The Examiner considers that it would have been obvious to the person skilled in the art to use silicon in the tablet according to Geyer et al., as used in Meyers et al., to obtain the tablet according to the invention.

In the tablet according to the invention, the active principle is coated and not intimately dispersed or dissolved in a pharmaceutically active lipid.

Thus, from Geyer, the man skilled in the art would not only have to add silicon, but also to replace an active principle intimately dispersed or dissolved in lipids by a coated active principle.

Meyer et al. teaches a very specific tablet comprising an uncured shearform matrix, in which a silica derivative can be used as glidant to adhere to the material in order to enhance flow properties by reducing interparticle friction, as indicated at column 13 lines 57-63.

Said function of the silica derivative results from the specific tablet comprising an uncured shearform matrix. There is thus no incentive for the man skilled in the art to add such a functional agent into the Geyer's tablet.

Claims 48 and 61 are thus inventive over Geyer et al. in view of Meyers et al.

Since claims 49 to 60 depend on claim 48 and since claims 62 to 74 depend on claim 61, they are also inventive.

It is submitted that the application is now in proper form for allowance and favourable consideration.

A Clean Version of Claims is attached.

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail, postage prepaid in an envelope addressed to: BOX AF, Commissioner for Patents, Washington, D.C. 20231 on October 3, 2002.

Alan H. Bernstein

CLEAN VERSION OF CLAIMS

48. Improved multiparticulate tablet which disintegrates in contact with the saliva in the mouth in less than 40 seconds, wherein it is based on particles of coated active principle which have intrinsic compression characteristics, and on a mixture of excipients being free of effervescent agents and the ratio of excipient mixture to coated active principle particles being 0.4 to 6 parts by weight, the mixture of excipients comprising: a disintegration agent; a soluble diluent agent with binding properties which consists of a directly compresssible polyol having less than 13 carbon atoms, with an average particle diameter of 100 to 500 μm; a lubricant; a permeabilizing agent, the proportion of disintegration agent being 1 to 15% by weight and the proportion of soluble agent being 30 to 90% by weight, based in each case on the weight of the tablet, said active principle not being intimately dispersed or dissolved in a pharmaceutically acceptable lipid.

49. Improved multiparticulate tablet according to claim 48, wherein the mixture of excipients further comprises lubricants, sweeteners, flavorings and colors.

50. Improved multiparticulate tablet according to claim 48, wherein the polyol having less than 13 carbon atoms is selected from the group consisting of mannitol, xylitol and maltitol.

51. Improved multiparticulate tablet according to claim 48, wherein the ratio of excipient mixture to coated active principle is 1 to 4 parts by weight.

52. Tablet according to claim 48, wherein the proportion of disintegration agent is 2 to 7% by weight and the proportion of soluble agent is 40 to 70% based in each case on the weight of the tablet.

53. Tablet according to claim 48, wherein the active principle is selected from the group consisting of aspirin, paracetamol and ibuprofen.

54. Tablet according to claim 48, wherein the disintegrating agent is selected from the group consisting of croscarmellose, crospovidone and mixtures thereof.

55. Tablet according to claim 48, wherein the permeabilizing agent is selected from the group consisting of silicas with a high affinity for aqueous solvents, maltodextrins, β-cyclodextrines and mixtures thereof.

56. Tablet according to claim 55, wherein the permeabilizing agent is precipitated silica.

57. Tablet according to claim 48, wherein the proportion of permeabilizing agent is 0.1 to 10% based on the weight of the tablet.

58. Tablet according to claim 57, wherein the proportion of permeabilizing agent is 0.5 to 5% based on the weight of the tablet.

59. Tablet according to claim 48, wherein the lubricant is selected from the group consisting of magnesium stearate, sodium stearyl flumarate, stearic acid, micronized polyoxyethylene glycol and mixtures thereof.

60. Tablet according to claim 50, wherein the sweetener is selected from the group consisting of aspartame, potassium acesulfame, sodium saccharinate, neohesperidin dihydrochalcone and mixtures thereof.

61. Improved multiparticulate tablet which disintegrates in contact with the saliva in the mouth in less than 40 seconds, wherein it is based on particles of coated active principle which have intrinsic compression characteristics, and on a mixture of excipients being free of effervescent agents and the ratio of excipient mixture to coated active principle particles being 0.4 to 6 parts by weight, the mixture of excipients comprising: a disintegration agent; at least two soluble diluent agents with binding properties which consists of a polyol having less than 13 carbon atoms and at least one diluent agent being in the form of the directly compressible product with an average particle diameter of 100 to 500 μm, and at least one diluent agent being in the form of a powder with an average particle diameter of less than 100μm, the ratio of directly compressible polyol to powder polyol being 99/1 to 20/80; a lubricant; a permeabilizing agent, the proportion of disintegration agent being 1 to 15% by weight and the proportion of soluble agent being 30 to 90% by weight, based in each case on the weight of the tablet, said active principle not being intimately dispersed or dissolved in a pharmaceutically acceptable lipid.

62. Improved multiparticulate tablet according to claim 61, wherein the mixture of excipients further comprises lubricants, sweeteners, flavorings and colors.

63. Improved multiparticulate tablet according to claim 61, wherein the polyol having less than 13 carbon atoms is selected from the group consisting of mannitol, xylitol, sorbitol and maltitol.

64. Improved multiparticulate tablet according to claim 61, wherein the ratio of excipient mixture to coated active principle is 1 to 4 parts by weight.

65. Improved multiparticulate tablet according to claim 61, wherein the proportion of directly compressible polyol to powder polyol is 80/20 to 20/80.

66. Tablet according to claim 61, wherein the proportion of disintegration agent is 2 to 7% by weight and the proportion of soluble agent is 40 to 70% based in each case on the weight of the tablet.

67. Tablet according to claim 61, wherein the active principle is selected from the group consisting of aspirin, paracetamol and ibuprofen.

68. Tablet according to claim 61, wherein the disintegrating agent is selected from the group consisting of croscarmellose, crospovidone and mixtures thereof.

69. Tablet according to claim 61, wherein the permeabilizing agent is selected from the group consisting of silicas with a high affinity for aqueous solvents, maltodextrins, β-cyclodextrines and mixtures thereof.

70. Tablet according to claim 69, wherein the permeabilizing agent is precipitated silica.

71. Tablet according to claim 61, wherein the proportion of permeabilizing agent is 0.1 to 10% based on the weight of the tablet.

72. Tablet according to claim 71, wherein the proportion of permeabilizing agent is 0.5 to 5% based on the weight of the tablet.

73. Tablet according to claim 61, wherein the lubricant is selected from the group consisting of magnesium stearate, sodium stearyl flumarate, stearic acid, micronized polyoxyethylene glycol and mixtures thereof.

74. Tablet according to claim 63, wherein the sweetener is selected from the group consisting of aspartame, potassium acesulfame, sodium saccharinate, neohesperidin dihydrochalcone and mixtures thereof.